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SEP 25 1996

Attachment 4

SUMMARY OF SAFETY AND EFFECTIVENESS

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DEVICE NAME: INCSTAR 25-Hydroxyvitamin D ^{125}I RIA

CLASSIFICATION NAME: 25-Hydroxyvitamin D Test System

APPLICANT: INCSTAR Corporation
1990 Industrial Boulevard
Stillwater, MN 55082-0285

DATE: July 26, 1995

The INCSTAR 25-Hydroxyvitamin D ^{125}I RIA Kit is intended for the quantitative measurement of 25-hydroxyvitamin D and other hydroxylated vitamin D metabolites in human serum or plasma to be used in the assessment of vitamin D sufficiency.

This assay requires serum or plasma samples to be extracted with acetonitrile to free vitamin D and its metabolites which are almost completely associated with binding proteins as well as remove lipids which would interfere with the assay. Calibrators (kit standards) containing known concentrations of 25-hydroxycholecalciferol (25-OH Vitamin D_3) in a human serum matrix are likewise extracted. The primary antibody (goat anti-25-OH vitamin D) selected for use in the assay demonstrates high affinity and equal cross-reactivity to both 25(OH)D_2 and 25(OH)D_3 but very low cross-reactivity to non-hydroxylated vitamin D_2 or D_3 and 1,25$(OH)_2$ D. The primary antiserum used in the assay does recognize several other dihydroxylated metabolites of vitamin D; however, these metabolites are found in relatively low concentrations in the circulation and are believed to be of minor biological importance. During the assay reaction, samples compete with an ^{125}I labeled analog of 25-OH D_3 for binding sites on the primary antiserum. Phase separation is accomplished using a donkey anti-goat, polyethylene glycol precipitating reagent. The amount of radioactivity contained in the resulting precipitate is inversely proportional to the concentration of 25-OH-D present in the sample.

The INCSTAR 25-Hydroxyvitamin D ^{125}I RIA Kit has been shown to be substantially equivalent to CPBA and HPLC methods used to determine levels of 25-OH-D. CPBA methods for measuring 25-OH-D have been used by commercial, clinical laboratories prior to the Medical Device Amendments of 1976. Furthermore, both methods have been compared to HPLC and have shown comparable results.

The INCSTAR 25-Hydroxyvitamin D ^{125}I RIA kit was compared to HPLC (High Pressure Liquid Chromatography), and CPBA (Competitive Protein Binding Assay) 25-OH-D methods. Various patient groups representing a wide range of 25-OH-D values were assayed using the INCSTAR kit, CPBA, and (in one study) HPLC. Results were analyzed using linear regression analysis.

The first study was performed by two external sites. Each site analyzed 36 serum samples using the INCSTAR kit, HPLC and CPBA. Results from both sites were combined (n=72). Values ranged from 4.7 to 186 ng/mL and gave the following results:

INCSTAR = 0.954 (HPLC) + 1.327; correlation coefficient = 0.993

INCSTAR = 0.998 (CPBA) - 0.639; correlation coefficient = 0.981

The second study, performed by one external site, analyzed 106 serum samples using the INCSTAR kit and CPBA. Results ranged from 7.4 to 461 ng/mL and gave the following results:

INCSTAR = 1.229 (CPBA) - 5.092; correlation coefficient = 0.942